

REMARKS

Claims 1-82 were pending in the application. Claims 22-24, 30-71, 73-82 were withdrawn from consideration as directed to non-elected inventions.

The specification has been amended to increase the line spacing in the tables.

Claims 1, 3, 25, 27, and 72 have been amended. Support for the amendments can be found throughout the specification as originally filed.

New claims 83-88 have been added. Support for new claims 83-88 can be found throughout the specification and claims as originally filed.

Upon entry of this amendment, claims 1-21, 25-29, 72, and 83-88 will be pending.

No new matter has been added.

Objections

Claims 25 and 72 stand objected to as being dependent upon non-elected claims. Claims 25 and 72 have been amended, rendering this objection moot.

The Office objected to the tables presented on pages 11, 26, 27, 60, and 61 of the specification as filed because the tables allegedly do not comply with 37 C.F.R. § 1.52(b) with respect to line spacing. Applicants respectfully disagree. However, in order to advance prosecution, Applicants have amended the specification so that the tables have line spacing of at least 1.5 lines.

In view of the foregoing, Applicants respectfully request that the objections to the specification and the claims be withdrawn.

Rejection under 35 U.S.C. § 101

Claims 1 to 21, 25, to 29 and 72 stand rejected under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by a specific, substantial and credible asserted utility or a well established utility. Applicants respectfully disagree.

Utility Examination Guidelines

The Utility Examination Guidelines require that a claimed invention have a specific, substantial and credible asserted utility, or, alternatively a well-established utility. As Applicants have asserted utilities that are specific, substantial and credible and well-established, the Utility Requirement has been satisfied. Applicants therefore respectfully request the withdrawal of the rejection under 35 U.S.C. § 101.

The Utility Examination Guidelines require a claimed invention to have a utility that is specific to the subject matter claimed (a "specific utility"). The present application recites at, for example, pages 37-42 of the specification that the claimed invention can be used, *inter alia*, to identify ligands and/or protein binding partners. Additionally, the polypeptides of the present invention can be used to generate antibodies useful to localize the protein *in vivo* or *in vitro*. For example, the specification teaches that nGPCR-2037 (SEQ ID NO: 1) is expressed in the central nervous system, with highest levels in all lobes of the cerebral cortex, cerebellum, corpus callosum, amygdala, substantia nigra, and the nucleus caudalis. The presence of nGPCR-2037 message was also apparent in the lymph node, testis and pituitary. Thus, antibodies generated against nGPCR-2037 can be used to identify the origin of cells and/or tissues as being from the brain and/or specific areas of the brain. Being able to identify specific cell types is also useful for identifying defects and abnormalities in the tissues by the absence or presence of staining of nGPCR-2037. Thus, there is no question that Applicants have asserted at least one specific utility and, in fact, have provided numerous specific utilities for the polypeptides of the present invention.

Additionally, the Office appears to be under the assumption that ***absolute*** certainty is required for a polynucleotide to have a specific utility. The standard applicable in this case is not, however, proof to certainty, but rather proof to reasonable probability. As the Supreme Court stated, applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner v. Manson*, 383 U.S. at 532. Although there may be numerous inventions that may arise from the present application, this standard does not justify the Office's stance that the present invention lacks a specific utility. Thus, Applicants have complied with the specific utility requirement.

The Claimed Invention Has A Substantial Utility

The Utility Examination Guidelines also require that a claimed invention have a utility that defines a real-world use (a "substantial utility"). Applicants teach, as described above, that the claimed invention can be used to make antibodies, identify ligands and other binding partners, such as other proteins that interact with the polypeptide (i.e., a G protein). Thus, it is clear that the claimed invention has real-world uses. All the uses described in the present application are real-world uses and stand in stark contrast to the "throw away" uses (e.g., landfill component or snake food) set forth in the utility guidelines. Thus, there is no question that Applicants have asserted at least one substantial utility and, in fact, have provided numerous substantial utilities. Accordingly, Applicants have complied with the substantial utility requirement.

The Claimed Invention Has A Credible Utility

In addition to a specific and substantial utility, the Utility Examination Guidelines require that such utility be credible (a "credible utility"). That is, whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided. Clearly, the numerous specific and substantial utilities asserted by Applicants are credible.

Assertions of utility are credible unless "(A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion." (See, Revised Interim Utility Guidelines Training Materials.) Further, the PTO is reminded that it **must** treat as true a statement of fact made by Applicants in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. All the utilities described for the polypeptide are based on sound logic. Furthermore, the utilities for the claimed isolated nucleic acid molecules, host cells and vectors are **not** inconsistent with the logic underlying the assertion that the polynucleotides and polypeptides are useful. Polypeptides and the

polynucleotides that encode them are useful to generate antibodies, identify ligands or protein partners, evaluate expression patterns, evaluate protein activity, etc. The Office has provided no evidence that the logic is seriously flawed or that the facts upon which these assertions are based are inconsistent with the logic underlying the assertions.

Furthermore, GPCR proteins have a well-established utility. Many medically significant biological processes are mediated by signal transduction pathways involving G-proteins and other second messengers, and G protein coupled seven transmembrane receptor proteins are recognized as important therapeutic targets for a wide range of diseases. According to a recently issued United States patent, nearly 350 therapeutic agents targeting GPCRs have been successfully introduced onto the market in only the last fifteen years. (See U.S. Patent No. 6,114,127, at col. 2, lines 45-50.) A recent journal review reported that most GPCR ligands are small and can be mimicked or blocked with synthetic analogues. That, together with the knowledge that numerous GPCRs are targets of important drugs in use today, make identification of GPCRs "a task of prime importance." (See, Marchese et al., Trends Pharmacol. Sci., 20(9): 370-5, 1999, attached hereto). Thus, the allegation that there is no well established utility for proteins of the class that the Applicants are now claiming is directly refuted by industry evidence.

In this respect, the G protein coupled receptor family is analogous to the chemical genus that was the subject of *In re Folkers*, 145 USPQ 390 (CCPA 1965) (Compound that belongs to class of compounds, members of which are recognized as useful, is considered useful under §101.) The Patent Office does not serve the public by attempting to substitute a formulaic analysis of § 101 for the established judgment of the biopharmaceutical industry as to what is "useful." If the Patent Office is aware of any well-grounded scientific literature suggesting that GPCR's are not useful, Applicants request that it be made of record.

Art-Recognized Utility

The Utility requirement may also be satisfied by an "Art Established Utility" which means that "a person of ordinary skill in the art would immediately appreciate why

the invention is useful based on the characteristics of the invention... and the utility is specific, substantial and credible." (M.P.E.P. §2107).

Applicants note for the record that the Patent Office apparently agrees with Applicants' reasoning that GPCRs are useful in that the Office has granted and apparently continues to grant patents to G-protein coupled receptors, their encoding polynucleotides and antibodies directed to them *in which no natural substrate or specific biological significance* is ascribed to the GPCR. Specifically, Applicants would like to bring the following US Patents to the Office's attention:

- 6,518,414** MacLennan "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims an isolated polynucleotide)
- 6,511,826** Li et al. "Polynucleotides Encoding Human G-Protein Chemokine Receptor (CCR5) HDGNR10" (Claims an isolated polynucleotide encoding a protein identified as a "chemokine receptor" with no specific chemokine identified)
- 6,372,891** Soppet et al. "Human G-Protein Receptor HPRAJ70" (Claims an antibody directed to a G-protein coupled receptor)
- 6,361,967** Agarwal et al. "AXOR10, A G-Protein Coupled Receptor" (Claims an isolated polynucleotide)
- 6,348,574** Godiska et al. "Seven Transmembrane Receptors" (Claims an antibody directed to a G-protein coupled receptor)
- 6,114,139** Hinuma et al. "G-Protein Coupled Receptor Protein and A DNA Encoding the Receptor" (Claims an isolated polynucleotide).
- 6,111,076** Fukusumi et al. "Human G-Protein Coupled Receptor (HIBCD07)" (Claims isolated polypeptide)
- 6,107,475** Godiska et al. "Seven Transmembrane Receptors" (Claims isolated polynucleotide and methods)
- 6,096,868** Halsey et al. "ECR 673: A 7-Transmembrane G-Protein Coupled Receptor" (Claims isolated polypeptide)
- 6,090,575** Li et al. "Polynucleotides Encoding Human G-Protein Coupled Receptor GPR1" (Claims isolated polynucleotide)
- 6,071,722** Elshourbagy et al. "Nucleic Acids Encoding A G-Protein Coupled 7TM Receptor (AXOR-1)" (Claims an isolated polynucleotide)
- 6,071,719** Halsey et al. "DNA Encoding ECR 673: A 7-Transmembrane G-Protein Coupled Receptor" (Claims an isolated polynucleotide)
- 6,060,272** Li et al. "Human G-Protein Coupled Receptors" (Claims isolated polynucleotide)
- 6,048,711** Hinuma et al. "Human G-Protein Coupled Receptor Polynucleotides" (Claims isolated polynucleotide)
- 6,030,804** Soppet et al. "Polynucleotides Encoding G-Protein Parathyroid Hormone Receptor HLTDG74 Polypeptides" (Claims isolated polynucleotide)

- 6,025,154** Li et al. "Polynucleotides Encoding Human G-Protein Chemokine Receptor HDGNR10" (Claims an isolated polynucleotide encoding a protein identified as a "chemokine receptor" with no specific chemokine identified)
- 5,998,164** Li et al. "Polynucleotides Encoding Human G-Protein Coupled Receptor GPRZ" (Claims isolated polynucleotide)
- 5,994,097** Lal et al. "Polynucleotide Encoding Human G-Protein Coupled Receptor" (Claims isolated polynucleotide)
- 5,958,729** Soppet et al. "Human G-Protein Receptor HCEGH45" (Claims isolated polypeptide)
- 5,955,309** Ellis et al. "Polynucleotide Encoding G-Protein Coupled Receptor (H7TBA62)" (Claims isolated polynucleotide)
- 5,948,890** Soppet et al. "Human G-Protein Receptor HPRAJ70" (Claims isolated polypeptide)
- 5,945,307** Glucksmann et al. "Isolated Nucleic Acid Molecules Encoding A G-Protein Coupled Receptor Showing Homology to The 5HT Family of Receptors" (Claims isolated polynucleotide)
- 5,942,414** Li et al. Polynucleotides Encoding Human G-Protein Coupled Receptor HIBEF51" (Claims isolated polynucleotide)
- 5,912,335** Bergsma et al. "G-Protein Coupled Receptor HUVCT36" (Claims isolated polynucleotide)
- 5,874,245** Fukusumi et al. "Human G-Protein Coupled Receptors (HIBCD07)" (Claims isolated polynucleotide)
- 5,871,967** Shabon et al. "Cloning of A Novel G-Protein Coupled 7TM Receptor" (Claims isolated polynucleotide)
- 5,869,632** Soppet et al. "Human G-Protein Receptor HCEGH45" (Claims isolated polynucleotide)
- 5,856,443** MacLennan et al. "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims isolated polynucleotide)
- 5,834,587** Chan et al. "G-Protein Coupled Receptor, HLTEX11" (Claims isolated polypeptide)
- 5,776,729** Soppet et al. "Human G-Protein Receptor HGBER32" (Claims isolated polynucleotide)
- 5,763,218** Fujii et al. "Nucleic Acid Encoding Novel Human G-Protein Coupled Receptors" (Claims isolated polynucleotide)
- 5,756,309** Soppet et al. "Nucleic Acid Encoding A Human G-Protein Receptor HPRAJ70 and Method of Producing the Receptor" (Claims isolated polynucleotide)
- 5,585,476** MacLennan "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims isolated polynucleotide)
- 5,759,804** Godiska et al. "Isolated Nucleic Acid Encoding Seven Transmembrane Receptors" (Claims isolated polynucleotide and methods)

Applicants submit that these issued US Patents are evidence of an art recognized utility for G-protein coupled receptors whose natural ligand is unknown. If the Patent

Office's position is that issued patents are *not* sufficient evidence of art recognition then Applicants respectfully request that this position be made of record. In the alternative, if the Patent Office wishes to take the position that these issued patents are directed to non-statutory subject matter, then Applicants respectfully request that this position be made of record as well.

In view of the foregoing, Applicants respectfully requests that the rejection under 35 U.S.C. § 101 be withdrawn.

Rejections under 35 U.S.C. § 112

Claims 1-21, 25-29, and 72 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to adequately teach how to use the instant invention "for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101." (Office Action, page 6). Applicants respectfully disagree.

As discussed above, the present invention *is* supported by a specific, substantial, and credible asserted utility as well as a well-established utility. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claims 1-21, 25-29, and 72 stand rejected under 35 U.S.C. § 112, first paragraph, because allegedly the specification failed to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. According to the Office:

These claims encompass an isolated nucleic acid encoding a polypeptide comprising an amino acid sequence "homologous" to the amino acid sequence presented in SEQ ID NO:2 or 3 of the instant application...The instant specification, however, only contains an adequate written description of a single protein within the recited genus and this protein comprises the amino acid sequence presented in SEQ ID NO:3, which is contained within SEQ ID NO:2. No homologous protein is adequately described in the instant specification...Because the instant specification does not identify that structural feature or combination of features which define the genus of claimed polypeptides...as required by the first paragraph of 35 U.S.C. § 112 it does not provide adequate written support for the breadth of the instant claims.

(Office Action, page 7). Applicants respectfully disagree.

According to the M.P.E.P:

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.

(M.P.E.P § 2163). The pending claims demonstrate that Applicants were in possession of the claimed invention at the time the application was filed because the claims contain "descriptive means" that define the claimed invention.

For example, claim 1 recites, "An isolated nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence that is at least 85% homologous to SEQ ID NO:2 or SEQ ID NO:3" The term "at least 85% homologous to" would be readily understood by one of ordinary skill in the art to provide structural and functional characteristics of the invention and is further clarified on pages 8 and 13 of the present application.

Claims 83 refers to an isolated nucleic acid that is at least 90% homologous to SEQ ID NO:1. A person of ordinary skill in the art would understand that the "descriptive means" of the pending claims include that the isolated nucleic acid molecule is at least 90% homologous to SEQ ID NO:1. A person of ordinary skill in the art would understand that further "descriptive means" of the genus are provided in claim 81 (that the encoded protein is a seven transmembrane receptor) and in claim 84 (that the encoded polypeptide is a G-protein coupled receptor). Claim 85 also has "descriptive means" that define the genus of the claimed nucleic acid molecule. Claim 86 recites:

An isolated nucleic acid molecule comprising a nucleotide sequence wherein said isolated nucleic acid molecule hybridizes to the nucleotide sequence set forth in SEQ ID NO: 1 or the noncoding strand complementary thereto, under stringent hybridization conditions with the provision that the nucleic acid molecule comprises a nucleotide sequence that differs from the sequence set forth as SEQ ID NO: 1 or from its complementary strand by at least one nucleotide.

The "descriptive means" set forth in claim 86 allow a person of ordinary skill in the art to readily understand that the defining characteristics of the claimed invention. A person of ordinary skill in the art would understand that Applicants had possession of the claimed

invention. The "descriptive means" set forth clearly show possession of the claimed invention.

Thus, Applicants have clearly shown that they had possession at the time the application was filed. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

Claims 1-21, 25-29 and 72 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. According to the Office, "Claims 1 to 21, 25 to 29 and 72 are vague and indefinite in so far as they rely upon the term "an amino acid sequence homologous to a sequence selected from the group consisting of SEQ ID NO:2 to SEQ ID NO: 3" and for allegedly employing "the term nGPCR-2037 as a limitation." (Office Action, pages 9-10). Applicants respectfully disagree.

Applicants have amended the claims to further clarify the claim language, rendering the rejection moot. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1-21 and 25 to 29 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent Publication 2001/0016337 A1 (Elshourbagy *et al* published August 23, 2001, hereinafter "Elshourbagy"). According to the Office:

The Elshourbagy *et al.* patent publication provided a written description of the claimed nucleic acid in an application filed before the effective filing date of the instant application. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph with respect to the now claimed invention. Because the instant application does not meet the requirements of 35 U.S.C. § 112, first paragraph, for those reasons given above and the prior applications also do not meet those requirements, they are unavailable under 35 U.S.C. § 120.

(Office Action, page 11). Applicants respectfully disagree.

The present application claims the priority benefit of U.S. Serial No. 60/195,228, filed April 6, 2000 and U.S. Serial No. 60/251,313, filed December 5, 2000. The priority applications as filed satisfy the requirements of 35 U.S.C. § 112 and, therefore, the present application is entitled to the priority date of at least December 5, 2000. For example, SEQ ID NOs:1-3 are present in U.S. Serial No. 60/251,313, filed December 5, 2000 (hereinafter "'313 application"). The claims filed in the '313 application are similar to the claims filed in the present application. "Homologous" and ranges of homology are defined in the provisional application (see, for example, pages 9 and 14). The '313 application also describes host cells and vectors. Thus, it is clear that the provisional application satisfies 35 U.S.C. § 112, first paragraph. Therefore, Elshourbagy is not available as prior art against the present application.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 102 be withdrawn.

Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6928 to clarify any unresolved issues raised by this response.

Respectfully submitted,



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